

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Paul TARDI, *et al.*

Serial No.: 10/417,631

Filing Date: April 16, 2003

For: COMPOSITIONS FOR DELIVERY OF
DRUG COMBINATIONS

Confirmation No.: 6691

Group Art Unit: 1616

Examiner: Ali Soroush

DECLARATION OF LAWRENCE D. MAYER

UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Lawrence D. Mayer, declare as follows:

1. I am President and Head of Research of Celator Pharmaceuticals, Inc., the assignee herein. I have been actively engaged in drug delivery research, both academically and in industrial settings for over 22 years. A copy of my *curriculum vitae* is attached as Exhibit A.

2. I agree with the statement by the Examiner in his Office Action dated November 15, 2007, "...the state of the art is very high in terms of formulating the liposomal sustained release compositions..." Indeed there were numerous references in the art at the time

of the present application describing a wide range of approaches and methods for controlling the loading as well as release of liposomal agents with the latter being widely examined for a number of antineoplastic agents. Methods of modulating drug retention and release in multiple delivery vehicles, including liposomes and polymer-based nanoparticles, are well known to those of skill in the art. This literature includes an extensive compendium of data on actual release rates for a multiplicity of drugs from a multiplicity of particulate carriers.

3. Examples of methods for controlling liposomal drug release include:
 - a) the use of a transmembrane ion gradients, particularly pH gradients generated with, for example, citrate, ammonium sulfate or an ionophore as well as using various degrees of said pH gradients;
 - b) the use of transmembrane osmotic gradients of varying degrees;
 - c) modulating the class (*e.g.*, anionic, neutral, pegylated), acyl chain length and/or amount of individual phospholipids used in a mixture;
 - d) the addition of cholesterol;
 - e) altering the drug-to-lipid ratio;
 - f) selecting delivery vehicles with specific phase transition temperatures

4. Below is a list of references for each of the above categories. It should be noted that this list is only meant to provide representative methods and numerous other examples and related approaches were readily available:

a) Ionic Gradients

- i. Cullis, P.R., *et al.*, Influence of pH gradients on the transbilayer transport of drugs, lipids, peptides and metal ions into large unilamellar vesicles. *Biochim. Biophys. Acta* (1997) 1331:187-211.

- ii. Burke, T., and Gao, X., Stabilization of topotecan in low pH liposomes composed of distearoylphosphatidylcholine. *J. Pharm. Sciences* (1994) July; 83(7):967-969.
- iii. Bowman, N., *et al.*, Liposomal vincristine which exhibits increased drug retention and increased circulation longevity cures mice bearing P388 tumors. *Cancer Res.* (1994) June 1; 54:2830:2833.
- iv. Haran, G., *et al.*, Transmembrane ammonium sulfate gradients in liposomes produce efficient and stable entrapment of amphipathic weak bases. *Biochim. Biophys. Acta* (1993) Sept 19; 1151(2):201-215.
- v. Fenske, D.B., *et al.*, Ionophore-mediated uptake of ciprofloxacin and vincristine into large unilamellar vesicles exhibiting transmembrane ion gradients. *Biochim. Biophys. Acta* (1998) Nov 11; 1414(1-2):188-204.
- vi. Bowman, N., *et al.*, Optimization of the retention properties of vincristine in liposomal systems. *Biochim. Biophys. Acta* (1993) 1152:253-258.
- vii. Clerc, S., and Barenholz, Y., Loading of amphipathic weak acids into liposomes in response to transmembrane calcium acetate gradients. *Biochim. Biophys. Acta* (1995) Dec 13; 1240(2):257-265.
- viii. Redelmeier, T., *et al.*, Proton flux in large unilamellar vesicles in response to membrane potentials and pH gradients. *Biophys. J.* (1989) Aug; 56(2):385-393.
- ix. US Patent 5,077,056 (Published December 31, 1991) – see Example 1 Part A – “Active Loading Using Na⁺ /K⁺ Gradients”

b) Osmotic Gradients

- i. Mui, B.L., *et al.*, Influence of plasma on the osmotic sensitivity of large unilamellar vesicles prepared by extrusion. *J. Biol. Chem.* (1994) Mar 11;269(10).
- ii. Allen, T.M., and Cleland, L.G., Serum-induced leakage of liposome contents. *Biochim. Biophys. Acta* (1980) 597:418-426.

c) Lipid Composition

- i. Horowitz, A.T., *et al.*, *In vitro* cytotoxicity of liposome-encapsulated doxorubicin: dependence on liposome composition and drug release. *Biochim. Biophys. Acta* (1992) 1109:203-209.
- ii. Frezard, F., and Garnier-Sullerot, A., Permeability of lipid bilayer to anthracycline derivatives. Role of the bilayer composition and of the temperature. *Biochim. Biophys. Acta* (1998) 1389:13-22.
- iii. Lim, H.J., *et al.*, Role of drug release and liposome-mediated drug delivery in governing the therapeutic activity of liposomal mitoxantrone used to treat human A431 and LS180 solid tumors. *J. Pharmacol. Exp. Ther.* (2000) Jan;-292(1):337-345.
- iv. Forssen, E.A., and Tokes, Z.A., Improved therapeutic benefits of doxorubicin by entrapment in anionic liposomes. *Cancer Res.* (1983) Feb; 43:546-550.

d) Cholesterol Content

- i. Dos Santos, N., *et al.*, Improved retention of Idarubicin after intravenous injection obtained for cholesterol-free liposomes. *Biochim. Biophys. Acta* (2002) Jan; 1561:188-201.
- ii. Ogiwara-Umeda, I., and Kojima, S., Cholesterol enhances the delivery of liposome-encapsulated gallium-67 to tumors. *Eur. J. Nucl. Med.* (1989) 15:612-617.
- iii. Fielding, R.M., and Abra, R.M., Factors affecting the release rate of terbutaline from liposome formulations after intratracheal instillation in the guinea pig. *Pharm. Res.* (1992) Feb; 9(2):220-223.

e) Drug-to-Lipid Ratio

- i. Mayer, L., *et al.*, Influence of vesicle size, lipid composition, and drug-to-lipid ratio on the biological activity of liposomal doxorubicin in mice. *Cancer Res.* (1989) Nov. 1; 49:5922-5930.

f) Phase Transition Temperature

- i. Hays, L.M., *et al.*, Factors affecting leakage of trapped solutes from phospholipid vesicles during thermotropic phase transitions. *Cryobiology* (2001) Mar; 42(2):88-102.
- ii. Hayashi, H., *et al.*, Temperature-controlled release property of phospholipid vesicles bearing a thermo-sensitive polymer. *Biochim. Biophys. Acta* (1996) 1280:127-134.
- iii. Anyarambhatla, G., and Needham, D., Enhancement of the phase transitions permeability of DPPC liposomes by incorporation of MPPC: A new temperature-sensitive liposome for use with mild hyperthermia. *J. Liposome Res.* (1999) 9(4):491-506.
- iv. Kong, G., *et al.*, Efficacy of liposomes and hyperthermia in a human tumor xenograft model: Importance of triggered drug release. *Cancer Res.* (2000) Dec. 15; 60:6950-6957.

5. In addition, a similar database existed at the time of the invention describing methods for controlling drug release from natural and synthetic non-liposomal delivery vehicles including micelles, nanoparticles, microspheres and drug-polymer conjugates. Below is a list of references which detail various methods for controlling the release of therapeutic agents from non-liposomal delivery vehicles:

- a) Genta, I., *et al.*, Different molecular weight chitosan microspheres: influence on drug loading and release. *Drug Dev. Ind. Pharm.* (1998) Aug; 24(8):779-784.

- b) Kim, H., and Fassihi, R., Application of binary polymer system in drug release rate modulation. 2. Influence of formulation variables and hydrodynamic conditions on release kinetics. *J. Pharm. Sci.* (1997) Mar; 86(3):323-328.
- c) Kawaguchi, T., *et al.*, Control of drug release with a combination of prodrug and polymer matrix: Antitumor activity and release profiles of 2',3'-Diacyl-5-fluoro-2'-deoxyuridine from Poly(3-hydroxybutyrate) microspheres. *J. Pharm. Sci.* (1992) June; 81(6):508-512.
- d) Anderson, B.C., *et al.*, Understanding drug release from poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) gels. *J. Control Release* (2001) Jan 29; 70(1-2):157-167.
- e) Muller, R.H., *et al.*, Solid lipid nanoparticles (SLN) for controlled drug delivery – A review of the state of the art. *Eur. J. Pharm. Biopharm.* (2000) Jul; 50(1):161-177.

6. Not only does the art describe various release rates for various drugs in various combinations, the above-cited documents also describe factors that can be controlled in predictable ways to accelerate or decelerate the release of any particular drug, such as a lipophilic drug, a hydrophilic drug, a charged drug or a neutral drug. For example, the rate of release of a lipophilic drug can be decelerated by employing phospholipids with longer acyl chains and can be controlled by adjusting the pH of the internal solution.

7. While the Examiner acknowledges that there is significant skill in the state of the prior art for controlling drug release of single drugs from drug delivery vehicles, he asserts in the November 15, 2007 Office Action that the state of the prior art is not high in terms of "...releasing the two neoplastic agents in the same non-antagonistic ratios." Actually the amount of knowledge of this subject was high at the time of the invention, but experiments were not

reported in the prior art until the present invention, since the knowledge that *ratios* are important AND must be maintained *in vivo* was never appreciated in the art. Therefore the known methods of controlling drug release were never applied to coordinating the release of drug combinations even though practitioners knew how to do it. Once the desirability of controlling ratios was revealed as a result of the present invention, those of skill in the art are able to use the abundant references available to construct delivery vehicles with matched release kinetics of two active agents thereby controlling their ratio after *in vivo* administration.

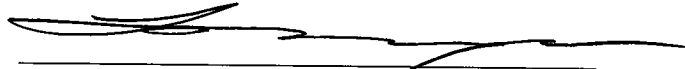
8. For drugs with dissimilar characteristics in which a single delivery vehicle coordinating release of the two drugs is not ideal as described in the specification (paragraphs 0023-0024, 0115, 0117 and 0130), two different carriers modulating the release kinetics of each drug individually can be designed to coordinate the ratio in the blood as demonstrated in Examples 8, 12, and 15 in the specification. The two drug-containing delivery vehicles can be mixed and co-administered *in vivo*. Thus, for example, a combination of a negatively charged drug with a positively charged one might be handled in this way. Coordinated release both from co-encapsulated drugs and drugs formulated separately is illustrated in Examples 8-9, 12-13 and 15-16.

9. Given the breadth of methods available in the prior art for controlling drug release, there are multiple features of each delivery vehicle which could be readily designed to achieve the coordinated release of two encapsulated agents whether co-encapsulated or encapsulated in separate delivery vehicles such that a desired synergistic ratio is maintained in the blood. This could be achieved without undue experimentation based on the extensive data-

base on actual drug release rates from drug delivery vehicles available in the literature for a wide range of drug classes and delivery vehicles.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Vancouver, CANADA, on January 14, 2008



Lawrence D. Mayer

Curriculum Vitae

DR. LAWRENCE D. MAYER

EXHIBIT A

EDUCATION

- Ph.D. Biochemistry (1983) University of Minnesota, Dr. Gary L. Nelsestuen, Supervisor
Thesis: Protein-Membrane Interactions Involved in the Prothrombinase System
- B.Sc. Majors in both Chemistry and Biology (1978, *Summa Cum Laude*) Wartburg College

PROFESSIONAL EMPLOYMENT

- 2003-Present **Founder, President and Head of Research, Celator Pharmaceuticals**
- 1999-2002 **Founder, President and Chief Executive Officer, Celator Pharmaceuticals**
- 2004-Present **Adjunct Scientist, BC Cancer Agency**
- 1992-Present **Adjunct Professor, Faculty of Pharmaceutical Sciences, University of B.C.**
- 1992-2003 **Senior Research Scientist, Division of Medical Oncology, B.C. Cancer Agency**
Research programs in the development of liposomal drug delivery systems, multidrug resistance and novel chemotherapeutic agents. Graduated 7 Ph.D. students, 3 M.Sc. students and supervised 16 postdoctoral fellows. Awarded over \$4M in research funding.
- 1999-2001 **Research Supervisor, Experimental Medicine, University of B.C.**
- 1992-2002 **Director, Investigational Drug Program, B.C. Cancer Agency**
Established and directed translational research and development activities of the Investigational Drug Program including GMP production of clinical supplies in the BCCA clean room facility and GLP testing. Co-ordinated proposals for preclinical and clinical testing of new anticancer agents for outside companies as well as development programs for agents generated within the Agency.
- 1990-1992 **Program Director, QLT Inc.**
Project manager for topical photosensitizer development program. Responsible for implementation of Quality Management system to ensure compliance with HPB and FDA regulatory requirements. Also responsible for directing formulation efforts of topical photosensitizers, coordinating activities between various departments (toxicology, pharmacology, clinical, *etc.*), preparing budget estimates and project administration. Member of Development Management Group responsible for establishing short term and long term corporate drug development strategy.
- 1987-1990 **Scientific Director, The Canadian Liposome Co. Ltd.**
Project leader of lead liposomal anticancer agent (TLC D-99) at CLC and its parent company The Liposome Co., Inc. (Princeton, N.J.). Responsible for coordinating R&D activities with current time tables for ongoing clinical trials and anticipated production requirements for future trials. Participated in preparing IND submissions to US FDA and Canadian HPB for clinical testing of TLC D-99. Co-directed research projects concerning the mechanism of action of liposomal anticancer pharmaceuticals. Responsible for developing budget requirements for active research projects.

1986-1987 **Research Associate, Biochemistry Dept., University of B.C.**

1983-1986 **Canadian MRC Postdoctoral Fellow, Biochemistry Department, University of B.C.**

AREAS OF SPECIAL INTEREST AND ACCOMPLISHMENTS

- Spearheaded the translation of Celator's CombiPlex fixed-drug ratio combination chemotherapy technology from the lab into the clinic, resulting in two products being evaluated in clinical trials.
- Part of Celator Senior Management team responsible for securing \$10MCDN Series A and \$40MUS Series B Venture Capital Financings
- Established new paradigm for developing drug combinations for cancer chemotherapy where synergistic drug:drug ratios are fixed inside liposomes for delivery to tumors. This allows drug combinations to be developed based on maximum efficacy rather than on tolerability.
- Co-founder of Celator Technologies as a spin-off of BCCA laboratory focussed on delivery of drug combinations
- Identified novel applications for and characterized the molecular and therapeutic activities of Bcl-2 antisense oligonucleotides used to chemosensitize human solid tumor xenografts which were implemented by Genta, the company developing Genesense.
- Established novel liposome delivery platform based on reactive, cholesterol-free membranes for enhanced disease site-selective activity.
- Identified enhanced lung cancer antitumor activity of vinca alkaloid derivative anhydrovinblastine and led translational research activities that resulted in IND submission for Phase I clinical testing.
- Discovered and characterized use of liposomal anticancer drug formulations in combination with P-glycoprotein inhibitors to effectively treat multidrug resistant tumors, an approach that was validated in later clinical trials.
- Led discovery and translational research activities to develop an optimized liposomal vincristine formulation and led preparation of the IND submission.
- Played leading role in basic and applied research for development of liposomal doxorubicin formulation currently approved for market use in Europe.
- Established and directed operations of the Investigational Drug Program at the BC Cancer Agency. This Program has been granted an Establishment License by the Canadian TPP as a GMP manufacturing clean room and testing facility for clinical trial supplies. This is the only academic center in Canada to hold such accreditation.

HONOURS AND AWARDS

- Nomination in the Ernst & Young Entrepreneur of the Year awards program, in recognition of determination and inspiration in building a thriving business – and a strong and vibrant country (2003)
- Canadian Medical Research Council Postdoctoral Fellow (1983-1986)
- Dissertation Fellowship, University of Minnesota (1982)
- Wayne Page Memorial Outstanding Student-Athlete Award, Wartburg College (1977)

TEACHING

Areas of special interest and accomplishments

- Worked on course coordination committee to develop Cancer Biology graduate course (Path 500)
- Active yearly participation in training of undergraduate students through summer research programs with Faculty of Pharmaceutical Sciences, Pharmacology Dept. and Biochemistry Dept. at UBC

Courses Taught at UBC

Session	Course Number	Scheduled Hours	Class Size	Hours Taught			
				Lectures	Tutorials	Labs	Other
1996-1997	MedGen 421		150	4			
1996-1997	Path 531		17	4			
1997-1998	MedGen 421		150	4			
1997-1998	Path 531		13	4			
1997-1998	Path 548		7	3			
1998-1999	MedGen 421		150	4			
1999	Phar 414				40		
1999-2000	Phar 510		12	8			
2001	Phar 550		50	4			
2001	Phar 414				30		

Graduate students supervised: 7

Students co-supervised: 3

Member of supervisory committees: 12

Postdoctoral fellows supervised: 17

SUMMARY OF GRANTS & CONTRACTS

Total # of grants/contracts held: 29

Range of years: 1992 -- 2006

Total amount of grant money: \$9,345,248

INVITED PRESENTATIONS

- "Association of prothrombin, Factor X and Factor V with phospholipid monolayers" FASEB meetings, Chicago, Illinois, May 1982.
- "Protein-membrane interactions involved in the prothrombinase system" Biomembranes Discussion Group, University of British Columbia, December 1982.

- "Influence of transmembrane ion gradients on the transbilayer distribution of dibucaine" Pharmacology Seminar Series, University of British Columbia, October 1985.
- "Optimization of the therapeutic activity of liposomal doxorubicin" FASEB Liposomal Drug Delivery Conference, Saxton, Vermont, July 1987.
- "Liposomal anticancer formulations with improved therapeutic potential" Oncology Experimental Therapeutics Seminar Series, Roswell Park Memorial Institute, Buffalo, New York, March 1990.
- "Development of liposomal vincristine preparations with improved therapeutic potential" Advanced Therapeutics Seminar Series, British Columbia Cancer Agency, Vancouver, B.C., October 1990.
- "Liposomes as intravenous drug delivery systems" Canadian Society of Hospital Pharmacists Annual General Meeting, Vancouver, B.C., November 1990.
- "Pharmacodynamics of liposomal anticancer agents" University of British Columbia, Faculty of Pharmaceutical Sciences Invited Lecture Series, Vancouver, B.C., March 1994.
- "Formulation, toxicity and pharmacology of liposomal doxorubicin" Liposome Research Days Conference, Vancouver, B.C., June 1994.
- "Pharmacology of vincristine encapsulated in sphingomyelin-cholesterol liposomes" AACR Annual General Meeting Discussion Session, Toronto, Ontario, March 1995.
- "Cellular pharmacology of verapamil in P388-ADR cells in vitro" AACR Annual General Meeting Discussion Session, Toronto, Ontario, March 1995.
- "Preclinical and clinical studies with liposomal vincristine" Third Drug Delivery Symposium, Shizuoka, Japan, June 1995.
- "Membrane Properties Control the Therapeutic Activity of Liposomal Vincristine" Fourth Liposomal Research Conference, Freiburg, Germany, August 1995.
- "The Use of Liposomes to Target Anticancer Agents to Solid Tumors" Gordon Research Conference on Drug Carriers in Biology and Medicine, Ventura, CA, February 1996.
- "Strategies for Optimizing Liposomal Anticancer Agents" PharmTech Conference, East Rutherford, N.J., September 1996.
- "The Use of Liposomes in Therapeutic and Mechanistic Studies of Multidrug Resistance" Canadian Multidrug Resistance Roundtable Meeting, Toronto, Ont., March 1997.
- "Current Trends in Cancer Chemotherapy" Bridging the Strait of Georgia Cancer Research Symposium, Sidney, B.C., May 1997.
- "Therapeutic and Mechanistic Studies on the Pharmacology of Multidrug Resistance" Univ. of British Columbia Dept. of Surgery Seminar Series, Vancouver, B.C., July 1997.
- "In Vivo Entrapment of Doxorubicin Utilising pH Gradient Liposomes" Gordon Research Conference on Drug Carriers in Biology and Medicine, Ventura, CA, February 1998.
- "Strategic Development of Biopharmaceuticals" Pictet Biotechnology Seminar, Vancouver, B.C., September 1998.
- "Designing Liposomal Anticancer Agents to Overcome MDR in Combination with the P-glycoprotein Inhibitor PSC 833" International Conference of Anticancer Research, Thessaloniki, Greece, October, 1998.
- "Optimization of Liposomal Anticancer Drug Formulations for Specific Therapeutic Applications" University of London Liposomes in Biomedical Applications Symposium, London, UK, Dec. 1999.
- "Therapeutic and Pharmacokinetic Properties of Doxorubicin combined with Bcl-2 Antisense Oligonucleotide Treatment" Poster Discussion Session, AACR Annual Meeting, San Francisco, CA, April 2000.
- "Matching Drug Release Kinetics with Therapeutic Applications for Liposomal Anticancer Drug Formulations" International Liposome Research Society Conference, Napa, CA, April 2000.
- "Characterization of a Novel Thermosensitive Liposomal Doxorubicin Formulation for Tumor Specific Drug Exposure" Congress of International Society of Hyperthermia Oncology, Taegu, Korea, April 2000.

- “Application of Liposomal Drug Delivery Systems for Treating Multidrug Resistant Tumors”
Pharmacology 2001, Vancouver, BC, March 2001.

CONFERENCE PARTICIPATION (ORGANIZER, KEYNOTE SPEAKER, ETC.)

- Session Chair, “Drug Delivery and Tumor Vascular Targeting” Amer. Assoc. Cancer Res. General Meeting, Philadelphia, PA, April 13, 1999.
- Session Chair, “Gene Targeting” Bridging the Strait of Georgia Cancer Symposium, Vancouver Island, 1998,
- Organizer, Bridging the Strait of Georgia Cancer Symposium, Vancouver Island, 1996 and 1998.
- Session Chair, “Developments in Antisense Technologies”, Gordon Research Conference on Drug Carriers in Biology and Medicine, Ventura, CA, February, 1996.
- Session Chair, “Steric Stabilisation”, Fourth Liposomal Research Conference, Freiburg, Germany, August 1995.

MEMBERSHIPS ON SCHOLARLY SOCIETIES, INCLUDING OFFICES HELD AND DATES

- 2005-present: Editorial Academy of the *International Journal of Oncology* (invited)
- 2003-present: American Association for the Advancement of Science
- 1997-present: International Liposome Society
- 1994-present: Parenteral Drug Association
- 1992-present: American Association of Cancer Research
- 1992-present: American Association of Pharmaceutical Sciences
- 1994-present: B.C. Biotechnology Alliance
- 1989-1993: Stanley Park Zoological Society (Elected member of Board of Directors)
- 1992-1994: Biopharmaceutical Innovation Resource Centre/Economic Regional Diversification Agreement Steering Committee

EDITORSHIPS

- 2001-Present: Journal of Experimental Therapeutics and Oncology
- 2001-Present: Molecular Cancer Therapeutics
- 1999-present: International Journal of Oncology

JOURNAL REVIEWER

- 2007-Present European Journal of Pharmaceutical Biopharmaceutics
- 2001-Present Molecular Cancer Therapeutics
- 2001-Present Journal of Pharmaceutical Research
- 1999-Present International Journal of Oncology
- 1998-Present Journal of Pharmaceutical Sciences
- 1998-Present: Cytometry
- 1997-Present Clinical Cancer Research
- 1996-Present: Molecular Pharmacology

- 1996-Present: European Journal of Pharmaceutical Science
- 1996-Present: Journal of Pharmacology and Experimental Therapeutics
- 1995-Present: International Journal of Cancer
- 1994-Present: European Journal of Cancer
- 1993-Present: Journal of Liposome Research
- 1992-Present: Journal of the American Chemical Society
- 1991-Present: Cancer Chemotherapy and Pharmacology
- 1991-Present: British Journal of Cancer
- 1990-Present: Journal of Biological Chemistry
- 1990-Present: Cancer Research
- 1987-Present: Biochemistry
- 1987-Present: Biochimica et Biophysica Acta

GRANTING AGENCY REVIEWER

- 2000-2004: Medical Research Council of Canada, Pharmaceutical Sciences Panel
- 1999-2004: Canadian Breast Cancer Research Foundation
- 1997, 1998, 2000: Alberta Cancer Board (External Reviewer)
- 1995-2001: National Cancer Institute of Canada, Panel G, Pharmacology,
- 1995, 1997, 1998: Medical Research Council of Canada (Pharmaceutics Panel, Cancer B Panel)
- 1995-1996: National Cancer Institute of Canada, Panel J

CONSULTANT (ORGANIZATION AND DATES)

- | | |
|---------------------------------------------------------------------------|-----------|
| • Photovision Pharmaceuticals, Inc., Jenkintwon, PA | 2000-2001 |
| • Duke University Hyperthermia Program (M. Dewhirst, Chair), Durham, N.C. | 1998-2002 |
| • Elan Pharmaceuticals, Inc., Ireland | 1998-1999 |
| • IGT Pharma, Inc., Vancouver, B.C. | 1997-2001 |
| • Angiogenesis Technologies, Vancouver B.C. | 1995-1997 |
| • QLT Phototherapeutics, Vancouver, B.C. | 1993-2000 |
| • Inex Pharmaceuticals, Corp., Burnaby, B.C. | 1993-1999 |

EXTERNAL EXAMINER

- University of Sydney (Pharmaceutical Sciences) June, 2000
- Simon Fraser University (Biology Department) July, 1998

OTHER SERVICE TO THE COMMUNITY

Guest Science Lectures at Mulgrave School, 1997, 1998, 2000
Mulgrave School (North Vancouver) Planning Committee, 1996-1997

PUBLICATIONS

Journals/Refereed

1. **Mayer LD** and Nelsestuen GL (1981) "Calcium and Prothrombin-Induced Lateral Phase Separation in Membranes" *Biochemistry* 20, 2457-2463.
2. Pusey ML, **Mayer LD**, Wei GJ, Bloomfield VA and Nelsestuen GL (1982) "Kinetic and Hydrodynamic Analysis of Blood Clotting Factor V-Membrane Binding" *Biochemistry* 21, 5262-5269.
3. **Mayer LD** and Nelsestuen GL (1983) "Membrane Lateral Phase Separation Induced by Proteins of the Prothrombinase Complex" *Biochim Biophys Acta*. 734, 48-53.
4. **Mayer LD**, Nelsestuen GL and Brockman HL (1983) "Prothrombin Association with Phospholipid Monolayers" *Biochemistry*, 22, 316-321.
5. **Mayer LD**, Pusey ML, Griep MA and Nelsestuen GL (1983) "Association of Blood Coagulation Factors V and X with Phospholipid Monolayers" *Biochemistry*, 22, 6266-6233.
6. Nayar R, **Mayer LD**, Hope MJ and Cullis PR (1984) "Phosphatidic Acid as a Calcium Ionophore in Large Unilamellar Vesicle Systems" *Biochim Biophys Acta*. 777, 343-346.
7. **Mayer LD**, Bally MB, Hope MJ and Cullis PR (1985) "Uptake of Dibucaine into Large Unilamellar Vesicles in Response to a Membrane Potential" *J. Biol. Chem.* 260, 802-808.
8. **Mayer LD**, Bally MB, Hope MJ and Cullis PR (1985) "Uptake of Antineoplastic Agents into Large Unilamellar Vesicles in Response to a Membrane Potential" *Biochim Biophys Acta*. 816, 294-302.
9. **Mayer LD**, Hope MJ, Cullis PR and Janoff AS (1985) "Solute Distributions and Trapping Efficiencies Observed in Freeze-thawed Multilamellar Vesicles" *Biochim Biophys Acta*, 817:193-196.
10. Richards RL, Habbersett RC, Scher I, Janoff AS, Schieren HP, **Mayer LD**, Cullis PR and Alving CR (1986) "Influence of Vesicle Size on Complement-Dependent Immune Damage to Liposomes" *Biochim Biophys Acta*. 855:223-230.
11. **Mayer LD**, Bally MB and Cullis PR (1986) "Uptake of Adriamycin into Large Unilamellar Vesicles in Response to a pH Gradient" *Biochim Biophys Acta*. 857:123-126.
12. **Mayer LD**, Hope MJ and Cullis PR (1986) "Vesicles of Variable Sizes Produced by a Rapid Extrusion Procedure" *Biochim Biophys Acta* 858:161-168.
13. **Mayer LD**, Bally MB, Hope MJ and Cullis PR (1986) "Techniques for Encapsulating Bioactive Agents into Liposomes" *Chem. Phys. Lipids* 40, 333-345.
14. Hope MJ, Bally MB, **Mayer LD**, Janoff AS and Cullis PR (1986) "Generation of Multilamellar and Unilamellar Phospholipid Vesicles" *Chem. Phys. Lipids* 40, 89-107.

15. Wong KF, Parmar YI, **Mayer LD**, Pritchard PH and Cullis PR (1987) "Detection of Protein-free Lipoprotein Analogues with an Apolar Lipid Core by Freeze-etch Electron Microscopy" *Biochim Biophys Acta.* 921:411-414.
16. Brenner DE, Arakali AV, **Mayer LD**, Ginsberg RS and Kanter P (1988) "Comparison of Liposomal Doxorubicin and Free Doxorubicin Pharmacokinetics in Rabbit" *Clin. Pharmacol. Therapeut.* 43, 125.
17. **Mayer LD**, Wong KF, Menon K, Chong C, Harrigan PR and Cullis PR (1988) "Influence of Ion Gradients on the Transbilayer Distribution of Dibucaine in Large Unilamellar Vesicles" *Biochemistry* 27, 2053-2060.
18. Bally MB, **Mayer LD**, Loughrey H, Redelmeier T, Madden TD, Wong K, Harrigan PR, Hope MJ and Cullis PR (1988) "Dopamine Accumulation in Large Unilamellar Vesicle Systems Induced by Transmembrane Ion Gradients" *Chem. Phys. Lipids* 47, 97-107.
19. Janoff AS, Kurtz CL, Jablonski RL, Minchey SR, Boni LT, Gruner SM, Cullis PR, **Mayer LD** and Hope MJ (1988) "Characterization of Cholesterol Hemisuccinate and Alpha Tocopherol Hemisuccinate Vesicles" *Biochim Biophys Acta.* 941:165-175.
20. Balazsovits JAE, **Mayer LD**, Bally MB, Cullis PR, Ginsberg RS and Falk RE (1989) "Analysis of the Effect of Liposome Encapsulation on the Vesicant Properties, Acute and Cardiac Toxicities, and Antitumour Efficacy of Doxorubicin" *Cancer Chemother. Pharmacol.* 23, 81-86.
21. Redelmeier TE, **Mayer LD**, Wong KF, Bally MB and Cullis PR (1989) "Proton Transport in Large Unilamellar Vesicles in Response to Electrical Potentials and Ph Gradients" *Biophys. J.* 56, 385-393.
22. **Mayer LD**, Tai LCL, Ko DSC, Masin D, Ginsberg RS, Cullis PR and Bally MB (1989) "Influence of Vesicle Size, Lipid Composition and Drug-to-Lipid Ratio on the Biological Activity of Liposomal Doxorubicin" *Cancer Research* 49, 5922-5930.
23. Cullis PR, **Mayer LD**, Bally MB, Madden TD and Hope MJ (1989) "Generation and Loading of Liposomal Systems for Drug Delivery Applications" *Advanced Drug Delivery Reviews* 3, 267-282.
24. **Mayer LD**, Bally MB, Loughrey H, Masin D and Cullis PR (1990) "Liposomal Vincristine Preparations Which Exhibit Decreased Toxicity and Increased Anti-tumour Activity Against Murine L1210 and P388 Tumours" *Cancer Research* 50, 575-579.
25. Madden TD, Harrigan PR, Tai LCL, Bally MB, **Mayer LD**, Redelmeier TE, Loughrey HC, Tilcock CPS, Reinish LW and Cullis PR (1990) "The Accumulation of Drugs Within Large Unilamellar Vesicles Exhibiting a Proton Gradient: A Survey" *Chem. Phys. Lipids* 53, 37-46.
26. Bally MB, Nayar R, Masin D, Hope MJ, Cullis PR and **Mayer LD** (1990) "Liposomes with Entrapped Doxorubicin Exhibit Extended Blood Residence Times" *Biochim Biophys Acta.* 1023: 133-139.
27. Thies RL, Cowens W, Cullis PR, Bally MB and **Mayer LD** (1990) "Method for Rapid Separation of Liposome-Associated Doxorubicin from Free and Doxorubicin in Plasma" *Anal. Biochem.* 188, 65-71.

28. **Mayer LD**, Bally MB, Cullis PR, Wilson SL and Emmerman JT (1990) "Comparison of Free and Liposome Encapsulated Doxorubicin Entrapped Tumour Drug Uptake and Antitumour Efficacy in the SC115 Murine Mammary Tumour" *Cancer Letters* 53, 183-190.
29. **Mayer LD**, Tai LCL, Bally MB, Mitilenes GN, Ginsberg RS and Cullis PR (1990) "Characterization of Liposomal Systems Containing Doxorubicin Entrapped in Response to pH Gradients" *Biochim Biophys Acta.* 1025:143-151.
30. Bally MB, Nayar R, Masin D, Cullis PR and **Mayer LD** (1990) "Studies on the Myelosuppressive Activity of Doxorubicin Entrapped in Liposomes" *Cancer Chemotherapy and Pharmacology* 27, 13-19.
31. **Mayer LD**, Bally MB and Cullis PR (1990) "Strategies for Optimizing Liposomal Doxorubicin" *J. Liposome Res.* 4, 463-480.
32. Cullis PR, Bally MB, Madden TD, **Mayer LD** and Hope MJ (1991) "pH Gradients and Membrane Transport in Liposomal Systems" *TIBTECH* 9, 268-272.
33. Kanter PM, Bullard GA, Ginsberg RA, Pilkievicz FG, **Mayer LD**, Cullis PR and Pavelic ZP (1993) "Comparison of the Cardiotoxic Effects of Liposomal Doxorubicin (TLC D-99) Versus Free Doxorubicin in Beagle Dogs" *In Vivo* 7, 17-26.
34. Kanter PM, Bullard GA, Pilkievicz FG, **Mayer LD**, Cullis PR and Pavelic ZP (1993) "Preclinical Toxicology Study of Liposome Encapsulated Doxorubicin (TLC D-99): Comparison with Doxorubicin and Empty Liposomes in Mice and Dogs" *In Vivo* 7, 85-96.
35. Embree L, Gelmon KA, Lohri A, **Mayer LD**, Coldman AJ, Cullis PR, Palaitis W, Pilkievicz F, Hudon NJ, Heggie JR and Goldie JH (1993) "Chromatographic Analysis and Pharmacokinetics of Liposome Encapsulated Doxorubicin (TLC D-99) in Non Small Cell Lung Cancer Patients" *J. Pharmaceutical Sciences*, 82, 627-634.
36. **Mayer LD**, Nayer R, Thies RL, Bowman NL, Cullis PR and Bally MB (1993) "Identification of Vesicle Properties Which Enhance the Antitumour Activity of Liposomal Vincristine Against Murine L1210 Leukemia" *Cancer Chemother. Pharmacol.*, 33, 17-24.
37. Boman NL, **Mayer LD** and Cullis PR (1993) "Optimization of Vincristine Retention in Liposomes In Vitro and In Vivo" *Biochim Biophys Acta.* 1152:253-260.
38. Bally MB, Masin D, Nayar R, Cullis PR and **Mayer LD** (1994) "Transfer of Liposomal Drug Carriers from the Blood to the Peritoneal Cavity of Normal and Ascitic Tumors - Bearing Mice" *Cancer Chemother. Pharmacol.*, 34, 137-146.
39. Bowman NL, Masin D, **Mayer LD**, Cullis PR and Bally MB (1994) "Liposomal Vincristine Which Exhibits Increased Drug Retention and Increased Circulation Longevity Cures Mice Bearing P388 Tumors" *Cancer Res.* 54, 2830-2833.
40. **Mayer LD**, Cullis PR and Bally MB (1994) "The Use of Transmembrane pH Gradient-Driven Drug Encapsulation in the Pharmacodynamic Evaluation of Liposomal Doxorubicin" *J. Liposome Res.* 4, 529-553.

41. Kanter PM, Klavich GM, Ballard GA, King JM, Bally M, Brand M and **Mayer LD** (1994) "Liposome Encapsulated Vincristine: Preclinical Toxicologic and Pharmacologic Comparison with Free Vincristine and Empty Liposomes in Mice, Rats and Dogs" *Anticancer Drugs*, 5, 579-590.
42. Alaoui-Jamali M, Wang T, Chen DZ, **Mayer LD** and Batist G (1995) "Effect of Tumor Grafts on Doxorubicin Host Toxicity" *Cell. Pharmacology*, 2:29-33.
43. **Mayer LD**, Masin D, Nayar R, Boman NL and Bally MB (1995) "Pharmacology of Liposomal Vincristine in Mice Bearing L1210 Ascitic and B16/BL6 Solid Tumors" *British J. Cancer*, 71:482-488.
44. de Jong G, Gelmon KS, Bally MB, Goldie JG and **Mayer LD** (1995) "Modulation of Doxorubicin Resistance in P388/ADR Cells by R044-5912, a Tiapamil Derivative" *Anticancer Research*, 15:911-916.
45. Webb MS, Wheeler JJ, Bally MB and **Mayer LD** (1995) "Improved Retention of Cationic Drugs in Liposomes Containing the Cationic Lipid Stearylamine" *Biochim Biophys Acta*. 1238:147-155.
46. Webb MS, Harasym TO, Masin D, Bally MB and **Mayer LD** (1995) "Sphingomyelin-cholesterol Liposomes Significantly Enhance the Pharmaceutic and Therapeutic Properties of Vincristine in Murine and Human Tumor Models" *British J. Cancer*, 72:896-904.
47. **Mayer LD** and St-Onge G (1995) "Determination of Free and Liposome Associated Doxorubicin and Vincristine Levels in Plasma Under Equilibrium Conditions Employing Ultrafiltration Techniques" *Analytical Biochemistry*, 232:149-157.
48. Boman NL, Bally MB, Cullis PR, **Mayer LD** and Webb MS (1995) "Encapsulation of Vincristine in Liposomes Reduces Its Toxicity and Improves Its Anti-Tumor Efficacy" *J. Liposomes Res.*, 5:523-541.
49. **Mayer LD** (1996) "Optimized Activity of Liposomal Vincristine (LIPOVINC) Through Liposome Manipulations" *J. Liposome Res.* 6:203-206.
50. **Mayer LD**, Dougherty G, Harasym TO and Bally MB (1996) "The Role of Tumour-Associated Macrophages in the Delivery of Liposomal Doxorubicin to Solid Murine Fibrosarcoma Tumours" *J. Pharmacol. Exp. Therapeutics*, 280: 1406-1414.
51. Embree L, Gelmon K, Tolcher A, Hudon N, Heggie J, Dedhar C, Webb M, Bally M & **Mayer LD** (1997) "Validation of a High-Performance Liquid Chromatographic Assay Method for Quantification of Total Vincristine Sulfate in Human Plasma Following Administration of Vincristine Sulfate Liposome Injection." *J. Pharmaceut. Biomed. Anal.*, 16: 675-687.
52. Cullis PR, Hope MJ, Bally MB, Madden TD, **Mayer LD** and Fenske DB (1997) "Influence of pH Gradients on the Transbilayer Transport of Drugs, Lipids, Peptides and Metal Ions into Large Unilamellar Vesicles" *Biochim Biophys Acta*. 1331: 187-211.
53. Zhang, X, Burt, HM, Mangold, G, Dexter, D, Von Hoff, D, **Mayer, L** and Hunter, WL (1997) "Antitumor Efficacy and Biodistribution of Intravenous Polymeric Micellar Paclitaxel" *Anti-Cancer Drugs*, 8: 696-701.

54. Krishna R and **Mayer LD** (1997) "Liposomal Doxorubicin Circumvents PSC-833-Free Drug Interactions, Resulting in Effective Therapy of Multidrug-Resistant Solid Tumors" *Cancer Res.* 57: 5246-5253.
55. Krishna R, deJong G and **Mayer LD** (1997) "Pulsed Exposure of SDZ PSC 833 to Multidrug Resistant P388/ADR and MCF7/ADR Cells in the Absence of Anticancer Drugs Can Fully Restore Sensitivity to Doxorubicin" *Anticancer Res.* 17: 3329-3334.
56. Embree L, Gelmon K, Tolcher T, Hudon N, Heggie J, Dedhar C, Logan P, Bally MB and **Mayer LD** (1998) "Pharmacokinetic Behaviour of Vincristine Sulfate Following Administration of Vincristine Sulfate Liposome Injection" *Cancer Chemother. Pharmacol.* 41: 347-352.
57. Webb MS, Saxon D, Wong FMP, Lim HS, Bally MB, Choi LSL, Cullis PR and **Mayer LD** (1998) "Comparison of Different Hydrophobic Anchors Conjugated to Poly(ethylene glycol): Effects on the Pharmacokinetics of Liposomal Vincristine" *Biochim Biophys Acta.* 1372: 272-282.
58. Webb MS, Logan P, Kanter PM, St.-Onge G, Gelmon K, Harasym T, **Mayer LD** and Bally MB (1998) "Preclinical Pharmacology, Toxicology and Efficacy of Sphingomyelin/ Cholesterol Liposomal Vincristine for Therapeutic Treatment of Cancer" *Cancer Chemother. Pharmacol.* 42: 461-470.
59. Bally MB, Lim H, Cullis PR and **Mayer LD** (1998) "Controlling the Drug Delivery Attributes of Lipid-Based Drug Formulations" *J. Liposome Res.* 8(3):299-335.
60. **Mayer LD**, Reamer J and Bally MB (1998) "Intravenous Pretreatment with Empty pH Gradient Liposomes Alters the Pharmacokinetics and Toxicity of Doxorubicin through In Vivo Active Drug Encapsulation." *J. Pharma. Sci.* 88: 96-102.
61. Gelmon KA, Tolcher A, Diab AR, Bally MB, Embree L, Hudon N, Dedhar C, Ayers D, Burge C, Logan P and **Mayer LD** (1999) "Phase I Study of Liposomal Vincristine" *J. Clin. Oncol.* 17: 697-705.
62. Krishna R, McIntosh NL, Riggs KW and **Mayer LD** (1999) "Doxorubicin Encapsulated In Sterically Stabilized Liposomes Exhibits Renal and Biliary Clearance Properties That Are Independent of Valspodar (PSC 833) under Conditions That Significantly Inhibit Nonencapsulated Drug Excretion." *Clin. Cancer Res.* 5: 2939-2947.
63. Gelmon K, Eisenhower E, Bryce C, Tolcher A, **Mayer L**, Tomlinson E, Zee B, Blackstein M, Tomiak E, Yau J, Batist G, Fisher B, and Iglesias J (1999) "Randomized Phase II Study of High-Dose Paclitaxel with or without Amifostine in Patients with Metastatic Breast Cancer" *J. Clin. Oncol.*, 17(10): 3038-3047.
64. Krishna R and **Mayer LD** (1999) "In vitro Evaluation of Doxorubicin Cytotoxicity and Cellular Uptake in the Presence and Absence of Multidrug Resistance Modulators" *Pharm. Pharmacol. Commun.* 5: 511-517.
65. Krishna R and **Mayer LD** (1999) "The Use of Liposomal Anticancer Agents to Determine the Roles of Drug Pharmacodistribution and P-glycoprotein (PGP) Blockade in Overcoming Multidrug Resistance" *Anticancer Res.*, 19:2885-2892.

66. Saxon DN, **Mayer LD** and Bally MB (1999) "Liposomal Anticancer Drugs as Agents to be Used in Combination with Other Anticancer Agents: Studies on a Liposomal Formulation with Two Encapsulated Drugs" *J. Liposome Res.*, 9:507-522.
67. Krishna R, St.-Louis M and **Mayer LD** (2000) "Increased Intracellular Drug Accumulation and Complete Chemosensitization Achieved in Multidrug-Resistant Solid Tumors by Co-administering Valspodar (PSC 833) with Sterically Stabilized Liposomal Doxorubicin." *Int. J. Cancer*, 85:131-141.
68. Dragowska WH, Lopez de Menezes D, Sartor J and **Mayer LD** (2000) "Quantitative Fluorescence Cytometric Analysis of Bcl-2 Levels in Tumor Cells Exhibiting a Wide Range of Inherent Bcl-2 Protein Expression: Correlation with Western Blot Analysis" *Cytometry*, 40:346-352.
69. Newman MJ, Rodarte JC, Benbatoul KD, Romano SJ, Uyeda RT, Moran EJ, Dixon R, Tomlinson ES and **Mayer LD** (2000) "Discovery and Characterization of OC144-093, a Novel Inhibitor of P-Glycoprotein-Mediated Multidrug Resistance" *Cancer Res.*, 60:2964-2972.
70. Johnstone SA, Gelmon K, **Mayer LD**, Hancock RE and Bally MB (2000) "*In Vitro* Characterization of the Anticancer Activity of Membrane-Active Cationic Peptides. I. Peptide-Mediated Cytotoxicity and Peptide-Enhanced Cytotoxic Activity of Doxorubicin against Wild-Type and P-glycoprotein Over-Expressing Tumor Cell Lines" *Anti-Cancer Drug Design*, 15:151-160.
71. Chi KN, Wallis AE, Lee CH, Lopez de Menezes D, Sartor J, Dragowska V and **Mayer LD** (2000) "Effects of Bcl-2 Modulation with G3139 Antisense Oligonucleotide on Human Breast Cancer Cells Are Independent of Inherent Bcl-2 Protein Expression" *Breast Cancer Res. Treat.*, 63:199-212.
72. Lopes de Menezes D, Hudon N, McIntosh N and **Mayer LD** (2000) "Molecular and Pharmacokinetic Properties Associated with the Therapeutics of Bcl-2 Antisense Oligodeoxynucleotide G3139 Combined with Free and Liposomal Doxorubicin" *Clin. Cancer Res.*, 6: 2891-2902.
73. Krishna R and **Mayer LD** (2000) "Multidrug Resistance (MDR) in Cancer Mechanisms, Reversal Using Modulators of MDR and the Role of MDR Modulators in Influencing the Pharmacokinetics of Anticancer Drugs" *European J. of Pharma. Sciences*, 11:265-283.
74. Zhang L, Scott MG, Yan H, **Mayer LD**, Hancock REW (2000) "Interaction of Polyphemusin I and Its Structural Analogues with Bacterial Membranes, Lipopolysaccharide and Lipid Monolayer" *Biochemistry*, 39:14504-14514.
75. Chiu GNC, Bally MB and **Mayer LD** (2001) "Selective Protein Interactions with Phosphatidylserine Containing Liposomes Alter the Steric Stabilization Properties of Poly(ethylene glycol)" *Biochim Biophys Acta*. 1510:56-69.
76. **Mayer LD**, Lim KT and Hartley D (2002) "Identification of Two Distinct Intracellular Verapamil Pools that Contribute to the Modulation of Multidrug Resistant P388-ADR Cells Expressing P-Glycoprotein" *J. Exp. Therapeut. Oncol.*, 2:107-120.

77. Waterhouse DN, Tardi PG, **Mayer LD** and Bally MB (2001) "Changing Toxicity Profiles: A Comparison of Liposomal Formulations of Doxorubicin with Drug Administered in Free Form" *Drug Safety*, 24(12):903-920.
78. Johnstone SA, Masin D, **Mayer L** and Bally MB (2001) "Surface Associated Serum Proteins Inhibit the Uptake of Phosphatidylserine and Poly(ethylene glycol) Liposomes by Mouse Macrophages" *Biochim Biophys Acta*. 1513(1):25-37.
79. Krishna R, Webb MS, St. Onge G and **Mayer LD** (2001) "Liposomal and Non-Liposomal Drug Pharmacokinetics after Administration of Liposome-Encapsulated Vincristine and Their Contribution to Drug Tissue Distribution Properties" *J. Pharmacol. Exp. Therapeut.*, 298:1206-1212.
80. Krishna R, Chiu G and **Mayer LD** (2001) "Visualization of Bioavailable Liposomal Doxorubicin Using a Non-Perturbing Confocal Imaging Technique" *Histology Histopath*, 16:693-699.
81. Waterhouse DN, Dos Santos N, **Mayer LD** and Bally MB (2001) "Drug-Drug Interactions Arising from the Use of Liposomal Vincristine in Combination with Other Anti-Cancer Drugs" *Pharm. Res.*, 18(9):1331-5.
82. Li WM, Xue L, **Mayer LD** and Bally MB (2001) "Intermembrane Transfer of Polyethylene Glycol Modified Phosphatidylethanolamine as a Means to Reveal Surface Associated Binding Ligands on Liposomes" *Biochim Biophys Acta*. 1513:193-206.
83. **Mayer LD** and Shabbits JA (2001) "The Role for Liposomal Drug Delivery in Molecular and Pharmacological Strategies to Overcome Multidrug Resistance" *Cancer Metast. Reviews*, 20:87-93.
84. Hu Y, Dragowska WH, Wallis A, Duronio V and **Mayer LD** (2001) "Cytotoxicity Induced by Manipulation of Signal Transduction Pathways Is Associated with Down-regulation of Bcl-2 but Not Mcl-1 in MCF-7 Human Breast Cancer" *Breast Cancer Res. and Treatment*, 70:11-20.
85. Shabbits JA, Krishna R and **Mayer LD** (2001) "Molecular and Pharmacological Strategies to Overcome Multidrug Resistance" *Expert Review of Anticancer Therapy* 1(4):585-94.
86. Krishna R and **Mayer LD** (2001) "Modulation of P-Glycoprotein (PGP) Mediated Multidrug Resistance (MDR) Using Chemosensitizers: Recent Advances in the Design of Selective MDR Modulators" *Curr. Med. Chem. – Anti-Cancer Agents*, 1:163-174.
87. Guns ES, Bullock PL, Reimer MLJ, Dixon R, Bally M and **Mayer LD** (2001) "Assessment of the Involvement of CYP3A in the In Vitro Metabolism of a New Modulator of MDR in Cancer Chemotherapy, OC144-093, by Human Liver Microsomes." *Eur J Drug Metab Pharm*, Oct-Dec;26(4):273-82, 2001.
88. Denyssevykh T, Lestou VS, Knesevich S, Robichaud M, Salski C, Tan R, Gascoyne RD, Horsman DE and **Mayer LD** (2002) "Establishment and Comprehensive Analysis of a New Human Transformed Follicular Lymphoma B-Cell Line, Tat-1" *Leukemia*, 16:276-283.

89. Lopes de Menezes DE and **Mayer LD** (2002) "Pharmacokinetics of Bcl-2 Antisense Oligonucleotide (G3139) Combined with Doxorubicin in SCID Mice Bearing Human Breast Cancer Solid Tumor Xenografts" *Cancer Chemother. Pharmacol.*, 49:57-68.
90. Chiu GNC, Bally MB and **Mayer LD** (2002) "Effects of Phosphatidylserine on Membrane Incorporation and Surface Protection Properties of Exchangeable Poly(ethylene glycol)-Conjugated Lipids" *Biochim Biophys Acta.* 1560(1-2):37-50.
91. Shabbits JA and **Mayer LD** (2002) "P-Glycoprotein Modulates Ceramide-Mediated Sensitivity of Human Breast Cancer Cells to Tubulin-Binding Anticancer Drugs" *Mol Cancer Ther*, 1:205-213.
92. Li WM, **Mayer LD** and Bally MB (2002) "Prevention of Antibody-Mediated Elimination of Ligand-Targeted Liposomes by Using Poly(Ethylene glycol)-Modified Lipids" *J. Pharmacol. Exp. Therapeut.*, 300(3):976-983.
93. Guns ES, Denyssevykh T, Dixon R, Bally MB and **Mayer LD** (2002) "Drug Interaction Studies Between Paclitaxel (Taxol) and OC144-093 - A New Modulator of MDR in Cancer Chemotherapy." *Eur J Drug Metab Pharm*, 27(2):119-126.
94. Dos Santos N, **Mayer LD**, Abraham SA, Gallagher RC, Cox KAK, Tardi PG and Bally MB (2002) "Improved Retention of Idarubicin after Intravenous Injection Obtained for Cholesterol-Free Liposomes" *Biochim Biophys Acta.* 1561:188-201.
95. Abraham SA, Edwards K, Karlsson G, MacIntosh S, **Mayer LD**, McKenzie C and Bally MB (2002) "Formation of Transition Metal-Doxorubicin Complexes Inside Liposomes" *Biochim Biophys Acta.* 1565/1:41-54.
96. Allen C, Dos Santos N, Gallagher R, Chiu GNC, Shu Y, Li WM, Johnstone SA, Janoff AS, **Mayer LD**, Webb MS and Bally MB (2002) "Controlling the Physical Behavior and Biological Performance of Liposome Formulations through Use of Surface Grafted Poly(ethylene glycol)" *BioScience Reports*, 22(2):225-250.
97. Shabbits JA, Chiu GN and **Mayer LD** (2002) "Development of an In Vitro Drug Release Assay that Accurately Predicts In Vivo Drug Retention for Liposome-Based Delivery Systems." *Journal of Controlled Release* 84:161-170.
98. Fung VWH, Chiu GNC and **Mayer LD** (2003) "Application of Purging Biotinylated Liposome from Plasma to Elucidate the Influx and Efflux Processes Associated with Accumulation of Liposomes in Solid Tumors" *Biochim Biophys Acta.* 1611:63-69.
99. Shabbits JA and **Mayer LD** (2003) "Intracellular Delivery of Ceramide Lipids Via Liposomes Enhances Apoptosis In Vitro" *Biochim Biophys Acta.* 1612(1):98-106.
100. Lopes de Menezes DE, Hu Y and **Mayer LD** (2003) "Combined Treatment of Bcl-2 Antisense Oligodeoxynucleotides (G3139), P-glycoprotein Inhibitor (PSC833) and Sterically-Stabilized Liposomal Doxorubicin Suppresses Growth of Drug-resistant Growth of Drug-resistant Breast cancer in SCID Mice" *J. Exp. Therapeut. Oncol.* 3:72-82.

101. Hu YP, Cherton-Horvat G, Dragowska V, Baird S, Korneluk RG, Durkin JP, **Mayer LD** and LaCasse EC (2003) "Antisense Oligonucleotides Targeting XIAP Induce Apoptosis and Enhance Chemotherapeutic Activity against Human Lung Cancer Cells *in vitro and in vivo*" Clin. Cancer Res. 9:2826-2836.
102. Chiu GNC, Bally MB and **Mayer LD** (2003) "Targeting of Antibody Conjugated, Phosphatidylserine-Containing Liposomes to Vascular Cell Adhesion Molecule 1 for Controlled Thrombogenesis" Biochimica et Biophysica Acta. 1613(1-2):115-21.
103. Hu Y, Bally M, Dragowska WH and **Mayer LD** (2003) "Inhibition of Mitogen-activated Protein Kinase/Extracellular Signal-regulated Kinase Kinase Enhances Chemotherapeutic Effects on H460 Human Non-Small Cell Lung Cancer Cells through Activation of Apoptosis" Mol Cancer Ther. 2(7):641-9.
104. Ickenstein LM, Arfvidsson MC, Needham D, **Mayer LD** and Edwards K (2003) "Disc Formation in Cholesterol-Free Liposomes During Phase Transition" Biochimica Biophys Acta. 1614(2):135-8.
105. Shabbits JA, Hu Y and **Mayer LD** (2003) Minireview "Tumor Chemosensitization Strategies Based on Apoptosis Manipulations" Mol Cancer Ther. 2(8):805-813.
106. Shabbits JA and **Mayer LD** (2003) "High Ceramide Content Liposomes with In Vivo Antitumor Activity" Anticancer Research 23:3663-3669.
107. Abraham SA, McKenzie C, Masin D, Ng R, Harasym TO, **Mayer LD** and Bally MB (2004) "In vitro and In vivo Characterization of Doxorubicin and Vincristine Co-encapsulated within Liposomes through Use of Transition Metal Ion Complexation and pH Gradient Loading" Clinical Cancer Research, 10:728-738.
108. Waterhouse DN, Dragowska WH, Gelmon KA, **Mayer LD** and Bally MB (2004) "Pharmacodynamic Behavior of Liposomal Antisense Oligonucleotides Targeting Her-2/neu and Vascular Endothelial Growth Factor in an Ascitic MDA435/LCC6 Human Breast Cancer Model" Cancer Biology and Therapy 3(2):1-8.
109. Dos Santos N, Cox KA, McKenzie CA, van Baarda F, Gallagher RC, Karlsson G, Edwards K, **Mayer LD**, Allen C and Bally MB (2004) "pH Gradient Loading of Anthracyclines into Cholesterol-Free Liposomes: Enhancing Drug Loading Rates Through Use of Ethanol" Biochim Biophys Acta. 1661:47-60.
110. Hu YP, Krishan A, Nie WJ, Sridhar KS, **Mayer L** and Bally M (2004) "Synergistic Cytotoxicity of Pyrazoloacridine with Doxorubicin, Etoposide and Topotecan in Drug Resistant Tumor Cells" Clin. Cancer Res. 10(3):1160-9.
111. Fedoruk MN, Giménez-Bonafé P, Guns ES, **Mayer LD** and Nelson CC (2004) "P-Glycoprotein Increases the Efflux of the Androgen Dihydrotestosterone and Reduces Androgen Responsive Gene Activity in Prostate Tumor Cells" Prostate 59(1):77-90
112. Abraham SA, Edwards K, Karlsson G, Hudon N, **Mayer LD** and Bally MB (2004) "An Evaluation of Transmembrane Ion Gradient-Mediated Encapsulation of Topotecan Within Liposomes" J. Control Res. 96(3):449-461

113. Messerer CL, Ramsay EC, Waterhouse DN, Ng R, Simms E-M, Harasym N, Tardi P, **Mayer LD** and Bally MB (2004) "Liposomal Irinotecan: Formulation Development and Therapeutic Assessment in Murine Xenograft Models of Colorectal Cancer" *Clinical Cancer Research*, 10(19):6638-49.
114. Bally M, Tardi P, Harasym T, Harasym N, Swenson C, Janoff A, **Mayer LD** (2004) "Spotlight:CTI" *Controlled Release Society Newsletter*, 21, No 2.
115. Hu YP, Bebb G, Tan S, Ng R, Yan H, **Mayer LD** and Bally MB (2004) "Anti-Tumor Efficacy of Oblimersen Bcl-2 Antisense Oligonucleotide Alone and in Combination with Vinorelbine in Xenograft Models of Human Non-Small Cell Lung Cancer" *Clinical Cancer Research*, 10(22):7662-70
116. Abraham SA, Waterhouse DN, **Mayer LD**, Cullis PR, Madden TD and Bally MB (2005) "The Liposomal Formulation of Doxorubicin" *Methods Enzymol.* 391:71-97
117. Waterhouse DN, Madden TD, Cullis PR, Bally MB, **Mayer LD** and Webb MS (2005) "Preparation, Characterization, and Biological Analysis of Liposomal Formulations of Vincristine" *Methods Enzymol.* 391:40-57
118. Guns ES, Xie X, Fedoruk M, Madera C, Cowell S, **Mayer LD**, Skov K, Gleave ME and Koslowski P (2005) "pH modulation using CsCl enhances therapeutic effects of vitamin D in LNCaP tumour bearing mice" *The Prostate.* 64(3):316-22
119. Sandström MC, Ickenstein LM, **Mayer LD**, Edwards K (2005) "Effects of lipid segregation and lysolipid dissociation on drug release from thermosensitive liposomes" *Journal of Controlled Release.* 107(1):131-42
120. Ickenstein LM, Sandström MC, Mayer LD, Edwards K (2005) "Effects of phospholipid hydrolysis on the aggregate structure in DPPC/DSPE-PEG2000 liposome preparations after gel to liquid crystalline phase transition" *Biochim Biophys Acta – Biomembranes* (in press)
121. **Mayer LD**, Harasym TO, Tardi PG, Harasym, NL, Shew CR, Johnstone SA, Ramsay EC, Bally MB, Janoff AS (2006) "Ratiometric dosing of anticancer drug combinations: controlling drug ratios after systemic administration regulates therapeutic activity in tumor-bearing mice" *Mol Cancer Ther.* 5(7):1854-63
122. Webb MS, Johnstone S, Morris TJ, Kennedy A, Gallagher R, Harasym N, Harasym T, Shew CR, Tardi P, Dragawska WH, **Mayer LD**, Bally MB (2007) "In vitro and in vivo characterization of a combination chemotherapy formulation consisting of vinorelbine and phosphatidylserine" *Eur J Pharm Biopharm* 65 (3):289-299
123. Dicko A, Tardi P, Xie X, Mayer LD, (2007) "Role of copper gluconate/triethanolamine in irinotecan encapsulation inside liposomes" *Int J Pharm.* 37: 219-228.
124. Tardi P, Gallagher R, Johnstone S, Harasym N, Webb M, Bally MB and **Mayer LD**, (2007) "Coencapsulation of irinotecan and floxuridine into low cholesterol-containing liposomes that coordinate drug release in vivo" *Biochim. Biophys. Acta* 1768: 678-687

125. Harasym T, Tardi P, Harasym N, Harvie P, Johnstone S and **Mayer LD**, (2007) "Increased preclinical efficacy of irinotecan and floxuridine co-encapsulated inside liposomes is associated with tumor delivery of synergistic drug ratios" *Oncol Res.*, 16(8):361-74 PMID: 17913044
126. Saad W, Prud'homme B, Ansell S and **Mayer LD** (2007) "Drug nanoparticle formation via flash nanoprecipitation: conjugation to encapsulate and control the release of paclitaxel" *J. Amer. Assoc. Pharm. Sci.* (in press)
127. Batist, G, Louie A, Chi K, Chia S, Gelmon K, Jewish General Hospital, McGill University, Montreal, PQ, Canada, Celator Pharmaceuticals Inc., Princeton, NJ, Miller, W., Swenson C. Janoff A, **Mayer LD** (2007) "Ratiometric dosing of irinotecan (IRI) and floxuridine (FLOX) in a phase 1 trial: A new approach for enhancing the activity of combination chemotherapy." *Proc. American Society of Clinical Oncology* 25: 109s
128. **Mayer, LD**, and Janoff, AS, (2007) "Optimizing combination chemotherapy by controlling drug ratios." *Mol Interv.* Aug. 7 (4):216-23. PMID: 17827442

Journals/Non-refereed

1. **Mayer LD** (1998) "Future Developments in the Selectivity of Anticancer Agents: Drug Delivery and Molecular Target Strategies" *Cancer and Metastasis Reviews* 17:211-218.
2. **Mayer LD** (2000) "Pharmaceutical Drug Delivery Systems; Medicine's Trojan Horse" *Helix*, 9:48-55.
3. **Mayer LD**, Krishna R, Webb M and Bally MB (2000) "Designing Liposomal Anticancer Drug Formulations for Specific Therapeutic Applications" *J. Liposome Res.*, 10(2&3):99-115.

Books/Authoried

1. Cullis PR, Hope MJ, Bally MB, Madden TD and **Mayer LD** (1987) "Liposomes as Pharmaceuticals" *In*: *Liposomes, from Biophysics to Therapeutics*. (M Ostro, ed.) pp. 39-72, Marcel Dekker Inc., NY.
2. Bally MB, Hope MJ, **Mayer LD**, Madden TD and Cullis PR (1988) "Novel Procedures for Generating and Loading Liposomal Systems" *In*: *Liposomes as Drug Carriers*. (G Gregoriadis, ed.) pp. 841-853, John Wiley and Sons Ltd., NY.
3. **Mayer LD**, Bally MB, Madden TD and Cullis PR (1992) "pH Gradient Mediated Drug Entrapment in Liposomes" *In*: *Liposome Technology*, Vol. II. (G Gregoriadis, ed.) pp. 27-44, CRC Press, Inc., Boca Raton, FL.
4. Bally MB, **Mayer LD**, Hope MJ and Nayar R (1992) "Pharmacodynamics of Liposomal Drug Carriers: Methodological Considerations" *In*: *Liposome Technology*, Vol. III. (G Gregoriadis, ed.) pp. 27-42, CRC Press, Inc., Boca Raton, FL.

5. Hope MJ, Nayar R, **Mayer LD** and Cullis PR (1992) "Reduction of Liposome Size and Preparation of Unilamellar Vesicle by Extrusion Techniques" In: Liposome Technology, Vol. I. (G Gregoriadis, ed.) pp. 123-140, CRC Press, Inc., Boca Raton, FL.
6. **Mayer LD**, Gelmon K, Cullis PR, Boman NL, Webb MS, Embree L., Tolcher T and Bally MB (1995) "Preclinical and Clinical Studies With Liposomal Vincristine" In: Progress in Drug Delivery Systems, Vol. IV, (S. Hirota, ed.) pp. 151-161, Biomedical Research Foundation, Tokyo, Japan.
7. Boman NL, Cullis PR, Bally MB and **Mayer LD** (1996) "Preclinical and Clinical Activity of Liposomal Doxorubicin" In: Liposomes in Biomedical Applications (P.N. Shek, ed.) Academic Publishers, Australia, pp.85-103.
8. Boman NL, Cullis PR, **Mayer LD**, Bally MB and Webb MS (1997) "Liposomal Vincristine: The Central Role of Drug Retention in Defining Therapeutically Optimized Anticancer Formulations" In: Long Circulating Liposomes: Old Drugs, New Therapeutics, G. Storm and M. Woodle, Eds., Lands Bioscience, N.Y., pp 29-49.
9. Krishna R and **Mayer LD** (1998) "Applications of Liposome Technology to Overcome Multidrug Resistance in Solid Tumors" In: Targeting of Drugs 6: Strategies for Stealth Therapeutic Systems (Ed. G. Gregoriadis), Plenum Press, NY, pp. 95-107.
10. **Mayer LD**, Cullis PR and Bally MB (1998) "Designing Therapeutically Optimized Liposomal Anticancer Delivery Systems: Lessons from Conventional Liposomes" In: Medical Applications of Liposomes, D.D. Lasic and D Papahadjopoulos, eds., Elsevier, N.Y, pp. 231-257.
11. **Mayer LD**, Krishna R and Bally, MB (2001) "Liposomes for Cancer Therapy Applications" In: Polymeric Biomaterials, 2nd Edition (S. Dumitriu, ed.) Marcel Dekker (New York, NY), 823-841.
12. Tardi P, Ickenstein L, Bally M and **Mayer LD** (2001) "The Development of Liposomes for Enhanced Delivery of Chemotherapeutics to Tumors" In: Cancer Drug Discovery and Development: Tumor Targeting in Cancer Therapy, pp. 119-135 (M. Pagé, Ed), Humana Press Inc., Totowa, NJ.
13. Krishna R and **Mayer LD** (2001) "Modulation of p-glycoprotein (PGP) Mediated Multidrug Resistance (MDR) Using Chemosensitizers: Recent Advances in the Design of Selective MDR Modulators" In: Current Trends in Medicinal Chemistry – Anticancer Drugs, *in press*.
14. Waterhouse DN, Bally MB, **Mayer LD**, Madden TD, Cullis PR and Webb MS (2003) "Preparation, Characterization and Biological Analysis of Liposomal Formulations of Vincristine" In: Methods in Enzymology, *In Press*.
15. Abraham SA, Waterhouse DN, **Mayer L**, Cullis P, Madden T and Bally MB (2003) "Liposomal Formulations of Doxorubicin" In: Methods in Enzymology, *In Press*.
16. Harasym T, Tardi P, Johnstone S, **Mayer LD**, Bally MB and Janoff A (2007) "Fixed Drug Ratio Liposome Formulations of Combination Cancer Therapeutics" In Liposome Technology Third Edition Volume III Interactions of Liposomes with Biological Milieu. (G Gregoriadis, ed) pp. 25-46, Informa Healthcare USA, Inc. NY

Conference Proceedings

1. Cowens JW, Kanter P, Brenner DE, Ginsberg R, **Mayer L**, Bally M, Cullis P, Pavelic Z, Douglass H, Petrelli N, Karakousis C and Creaven PJ (1989) "Phase I Study of Doxorubicin Encapsulated in Liposomes" Proc. ASCO 8, 69, Abs. No. 268.
2. **Mayer LD**, Nayar R, Thies RL, Thomas NL, Cullis PR and Bally MB (1990) "The Influence of Vesicle Properties on the Antitumour Activity of Liposomal Vincristine" Proc. AACR 31, 427, Abs. No. 2538.
3. Nayar R, **Mayer LD**, Masin D, Cullis PR and Bally MB (1990) "Antitumor Activity of Liposomal Encapsulated Doxorubicin in Different Murine Tumor Models: Implications for Mechanisms of Action" Proc. AACR 31, 429, Abs. No. 2549.
4. Cowens JW, Creaven PJ, Brenner DE, Ginsberg R, Petrelli N, Huben R, Karakousis C, Douglass H, **Mayer L**, Bally M, Cullis P, Goolsby H and Solomon J (1990) "Phase I Study of Doxorubicin Encapsulated in Liposomes" Proc. ASCO 9, 87, Abs. No. 338.
5. Lohri A, Gelmon KA, Embree L, **Mayer L**, Cullis P, Saletan S and Goldie J (1991) "Phase I/II Study of Liposome Encapsulated Doxorubicin (TLC D-99) in Non-Small Cell Lung Cancer (NSCLC)" Proc. ASCO 10, 106, Abs. No. 292.
6. Embree L, Lohri A, Gelmon K, **Mayer L**, Cullis P, Pilkievicz F, Hudon N, Heggie J, and Goldie J (1991) "Liposome-Encapsulated Doxorubicin Pharmacokinetics in Patients with Non-Small Cell Lung Cancer" Proc. AACR 32, 4, Abs. No. 279.
7. Bally MB, **Mayer LD** and Nayar R (1991) "Peritoneal Influx of Intravenously Administered Liposomal Doxorubicin: A Model for Extravasation of Liposomal Drug Carriers" Proc. AACR 32, 74, Abs. No. 2337.
8. Batist G, **Mayer L**, Pilkievicz F, Wang T, Skrutkowska M, Zukiwski A, Ahlgren P, Skelton J, Gruner P and Leyland-Jones B (1991) "Liposomal Doxorubicin (TLC D-99) in Experimental and Clinical Breast Cancer is Effective and Less Toxic" Proc. AACR 32, 91, Abs. No. 1090.
9. Kanter PM, Pilkievicz FG, Pavelic Z and **Mayer L** (1991) "Comparison of the Cardiotoxic Effects of Liposomal Doxorubicin (TLC D-99) Versus Free Doxorubicin in Beagle Dogs" Proc. AACR 32, 122, Abs. No. 2266.
10. Logan PM, **Mayer LD**, Comiskey S, Randazzo T, Straight R, Dube J, Brown L and McCullough JL (1992) "Photodynamic Therapy of Papillomavirus Disease Using Topical Benzoporphyrin Derivative" Proc. Amer. Soc. Photobiol.
11. Gelmon KA, Embree L, Lohri A, **Mayer L**, Cullis P, Saletan S, Hudon N, Heggie J and Goldie J (1992) "Clinical and Pharmacokinetic Results of a Phase I/II Study of Liposome Encapsulated Doxorubicin (TLC D-99) in Non-Small Cell Lung Cancer (NSCLC)" Proc. NCI-EORTC Symposium.

12. **Mayer LD**, Harasym T, Masin D, Zhang GY and Bally MB (1994) "Role of Tumor Associated Macrophages in the Delivery of Liposomal Anticancer Agents to Tumors" Proc. AACR 35, 418, Abs. No. 2493.
13. **Mayer LD** and Hartley D (1995) "Identification of Two Distinct Intracellular Verapamil Binding Pools that Contribute to the Reversal of Multidrug Resistance in P388-ADR Cells" Proc. AACR 36, 341.
14. Webb MS, Masin D, Harasym T, Heggie J, Bally M and **Mayer L** (1995) "Formulation, Pharmacokinetic and Therapeutic Properties of Vincristine Entrapped in Sphingomyelin Cholesterol Liposomes" Proc. AACR 36, 306.
15. Zhang Z, Kim N, **Mayer LD**, Cruz T and Hunter W (1996) "In Vitro Evaluation of the Antitumour Activity of Orthovanadate and Vanadyl Sulfate". Proc. AACR 37,396.
16. Embree L, Gelmon KA, Tolcher T, Heggie JR, Hudon NJ, Dedhar C, Bally MB and **Mayer LD** (1996) "Clinical Pharmacokinetics of vincristine sulphate liposome injection (VSLI)". Proc. AACR 37,179.
17. Krishna R, deJong G, Masin D, and **Mayer LD** (1996). "Pharmacology of multidrug resistance (MDR) reversal by PSC 833 and improved in vivo activity when combined with liposomal doxorubicin". Proc. AACR 37,331.
18. Harris AL, Rodarte JC, Chang Y, Moran EJ, Mjalli AM, **Mayer LD**, Bally MB, Shapiro AB and Toyonaga BE (1996) "The use of combinatorial chemistry and high throughput screening to discover a novel and potent multi-drug resistance (MDR) reversing agent". Proc. AACR 37,410.
19. Toleikis PM, Zhang Z, Cruz TF and **Mayer LD** (1997) "Antitumor Activity of a Novel Vanadium Compound (NVC) in Pre-clinical Evaluations" Proc. AACR 38, 105.
20. Xue LY, Longman SA, **Mayer LD** and Bally MB (1997) "Enhanced Tumor Delivery of Liposomes: Is it Really a Function of Carrier Circulation Levels?" Proc. AACR 38,259.
21. Krishna R, Masin D and **Mayer LD** (1997) "Pharmacokinetics of Free and Liposomal Doxorubicin in the Presence and Absence of SDZ PSC 833 in Mice Bearing P388/ADR Solid Tumors" Proc. AACR 38, 593.
22. McIntosh NL, Bally MB, Schmidt BA, Gelmon KA, Tolcher TW and **Mayer LD** (1998) "Novel in vitro and in vivo Activity of the Vinca Alkaloid 3',4' dehydrovinblastine (AVLB)" Proc. AACR 39, 166.
23. Krishna R, McIntosh N, Masin D and **Mayer LD** (1998) "Effective therapy of multidrug resistant MDA435LCC6 solid tumor bearing RAG2 mice using liposomal doxorubicin and PSC 833: influence of lipid composition on antitumor activity" Proc. AACR 39, 75.
24. Krishna R and **Mayer LD** (1998) "Designing liposomal anticancer agents to overcome multidrug resistance (MDR) in combination with the P-glycoprotein inhibitor PSC 833" Anticancer Res. 18, suppl. 6C, 4913.

25. Newman MJ, Rodarte JC, Benbatoul KD, Romano SJ, Uyeda RT, Moran EJ, Ripka WR, Toyonaga B, Dixon R, Tomlinson ES and **Mayer LD** (1999) "Discovery and characterization of OC144-093, a novel inhibitor of P-glycoprotein-mediated multidrug resistance" Proc. AACR 40, 315, 1999.
26. Krishna R, McIntosh N, Riggs KW and **Mayer LD** (1999) "Influence of Liposomal encapsulation on the renal and hepatobiliary disposition of doxorubicin in the presence and absence of valspodar (PSC 833) Proc. AACR 40, 417, 1999.
27. Chi KN, Lee CH, Wallis AE and **Mayer LD** (1999) "Chemosensitivity of breast cancer cell lines in response to Bcl-2 down-regulation and p-glycoprotein inhibition" Proc. AACR 40, 592, 1999.
28. Newman MJ, Rodarte JC, Romano SJ, Ripka WC, Dixon R, Guns ES, Denyssevysh T and **Mayer LD** (2000) "Novel in vivo mechanism of action and lack of pharmacokinetic interaction with plasma paclitaxel by the P-glycoprotein inhibitor OC144-093" Proc. AACR 41, 398.
29. Lopez de Menezes DE, Hudon N, McIntosh N and **Mayer LD** (2000) "Therapeutic and pharmacokinetic properties of doxorubicin combined with Bcl-2 antisense oligonucleotide G3139 treatment" Proc. AACR 41, 642.
30. Dragowska WH, Lopes de Menezes DE, Sartor J and **Mayer LD** (2000) "Quantitative flow cytometric analysis of Bcl-2 levels in tumor cells exhibiting a wide range of inherent Bcl-2 protein expression: Correlation with western analysis" Proc. AACR 41, 653.
31. Lopez de Menezes DE and **Mayer LD** (2001) "Combination of Bcl-2 antisense oligodeoxynucleotide (G3139), P-glycoprotein inhibitor (PSC833) and liposomal doxorubicin can suppress the growth of drug-resistant human breast cancer xenografts in SCID mice" Proc. Amer. Assoc. Cancer Res. 42:154, Abs. 2018.
32. Saxon DN, Gelmon KA, **Mayer LD** and Bally MB (2001) "Anti-HER-2/Neu antisense oligonucleotides in the treatment of MDA435/LCC6 ascites tumors" Proc. Amer. Assoc. Cancer Res. 42, Abs. 3901.
33. Shabbits JA and **Mayer LD** (2001) "Differentiating between PDMP induced chemosensitization VIA drug transport and ceramide signaling pathways" Proc. Amer. Assoc. Cancer Res. 42:268, Abs. 4378.
34. Sartor JR, Dragowska WH, Masin D and **Mayer LD** (2001) "Bcl-2 levels in transfected breast carcinoma cell lines MCF-7 and MDA-435/LCC6: Effect on the growth characteristics and chemosensitivity to doxorubicin and taxol in vitro and in vivo" Proc. Amer. Assoc. Cancer Res. 42:303, Abs. 5010.
35. Dos Santos N, **Mayer L** and Bally M (2001) "Prolonged Circulation Longevity of the Anthracycline Idarubicin Encapsulated in Cholesterol-Free Liposomes" Proc. Amer. Assoc. Pharmaceut. Scientists, October 20-26, 2001, Abs.M2327.
36. Abraham SA, Edwards K, Karlsson G, **Mayer L** and Bally M (2001) "Formulation of Doxorubicin-Metal Chelates Inside the Liposome" Proc. Amer. Assoc. Pharmaceut. Scientists, October 20-26, 2001.

37. Chiu GN, Shabbits JA, Bally MB and **Mayer LD** (2001) "Exchangeability of Poly(ethylene Glycol)-Lipid Conjugates Regulates the Membrane Reactivity of Phosphatidylserine Containing Liposomes. AAPS Annual Meeting and Exposition, October 21-25, 2001, Denver, CO, USA. Abstract # W4358.
38. Hu Y, Dragowska V, Korneluk R, Cherton-Horvat G, Durkin J, Lacasse E and **Mayer L** (2002) "Antisense Oligonucleotides Targeting XIAP Induce Apoptosis and Enhance Therapeutic Activity Against Human Lung Cancer Cells when Combined with anticancer Drug In Vitro and In Vivo" American Association for Cancer Research 93rd Annual Meeting, San Francisco, April 6-10, 2002; Abs. #2856.
39. Dos Santos N, Cox KA, Allen C, Gallagher RC, Ickenstein L, **Mayer LD** and Bally MB (2002) "Ethanol Induced Increases in the Rate of Doxorubicin Loading in Cholesterol-Free Liposomes" Liposome Research Days Conference, Berlin-Buch, Germany, May 21-24, 2002. J. Liposome Res. 13(1), 64-65, 2002.
40. Ickenstein LM, Arfvidsson M, Edwards K, Karlsson G and **Mayer LD** (2002) "Drug Release Mechanisms in Thermosensitive Liposomes During Phase Transition", presented as a poster at the 8th Liposome Research Days Conference in Berlin-Buch, Germany, May 21-24, 2002.
41. Chiu GNC, Bally MB and **Mayer LD** (2002) "Designing Lipid-Based Therapeutics for the Induction of Tumor Specific Thrombosis" The First International Conference on Vascular Targeting, June 12-14, 2002, Cambridge, MA, USA.
42. Hu YP, Masin D, Tan S, Ng R, Yan H, Harasym N and **Mayer L** (2003) "Anti-Metastatic and Anti-Tumor Efficacy of G3139, a Bcl-2 Antisense Oligonucleotide, as Single Agent or in Combination with Vinorelbine, in Murine Orthotopic and Ectopic Xenograft Models of Human Non-Small Cell Lung Cancer" 94th Annual Meeting, Washington, July 11-15, 2003. Proceedings of the American Association for Cancer Research, 44 #6432.
43. Shabbits JA and **Mayer LD** (2003) "Intracellular Delivery of Ceramide Lipids via Liposomes Enhances Apoptosis In Vitro and In Vivo" 94th Annual Meeting, Washington, July 11-15, 2003. Proceedings of the American Association for Cancer Research, 44 #640.
44. Chiu GNC, Tan S, Warburton C, Waterhouse DN, Webb M, **Mayer LD** and Bally MB (2003) "Liposome Conjugated Herceptin®: Coupling of a therapeutic antibody to liposomes does not inhibit antibody mediated antitumor activity" 94th Annual Meeting, Washington, July 11-15, 2003. Proceedings of the American Association for Cancer Research, 44 #3664.
45. Harasym T, Shu Y, Suragh C, Shew C, Tardi P, Bally MB and **Mayer LD** (2004) "Significance of Drug Ratio in Defining Optimal Synergistic Interactions of Approved Anticancer Drug Combinations" American Association for Cancer Research 95th Annual Meeting, Orlando, Florida, March 27-31, 2004. Proceedings of the American Association for Cancer Research_45 #127
46. **Mayer LD**, Harasym T, Harasym N, Tardi P, Shu Y, Suragh C, Simms E-M and Bally MB (2004) "A Pharmaceutical Approach to Achieve Synergy In Vivo: A Fixed Ratio Formulation of Irinotecan and Floxuridine for Treatment of Colorectal Cancer" American Association for Cancer Research

95th Annual Meeting, Orlando, Florida, March 27-31, 2004. Proceedings of the American Association for Cancer Research 46 #126-127

47. **Mayer LD**, Harasym N, Harasym T, Tardi P, Shu Y, Suragh C, Simms E-M and Bally MB (2004) "The Therapeutic Activity of Fixed Ratio Formulations of Irinotecan and Floxuridine are Ratio Dependent: Therapeutic Assessment in the Capan-1 Human Pancreatic tumour Xenograft Model" American Association for Cancer Research 95th Annual Meeting, Orlando, Florida, March 27-31, 2004. Proceedings of the American Association for Cancer Research 47 #126
48. Ramsay E, Alnajim J, Anantha M, Denyssevysh T, Harasym T, Masin D, Tardi P, **Mayer LD** and Bally MB (2004) "Development and Characterization of a Fixed Ratio Formulation of Cisplatin and Irinotecan: In Vitro and In Vivo Activity Against the Human H460 Lung Carcinoma Model" Proc. American Association for Cancer Research 95th Annual Meeting, Orlando, Florida, March 27-31, 2004. Proceedings of the American Association for Cancer Research 48 #126
49. Ramsay E, Alnajim J, Anantha M, Dicko A, Harvie P, **Mayer LD**, Bally MB and Tardi P (2004) "A Novel Approach to Prepare a Liposomal Irinotecan Formulations that Exhibit Significant Therapeutic Activity In Vivo" American Association for Cancer Research 95th Annual Meeting, Orlando, Florida, March 27-31, 2004. Proceedings of American Association of Cancer Research 49 #148
50. Tardi P, Webb M, Dumont A, Gallagher R, Johnstone S, Harasym N, Harasym T, Shew C, Dragowska WH, **Mayer LD** and Bally MB (2004) "Therapeutic Potential of a Drug Combination Consisting of Vinorelbine Encapsulated in Liposomes Containing a Therapeutically Active Lipid, Phosphatidylserine: In Vitro and In Vivo Characterization" American Association for Cancer Research 95th Annual Meeting, Orlando, Florida, March 27-31, 2004. Proceedings of the American Association of Cancer Research 50 #145-146
51. Ramsay E, Alnajim J, Anantha M, Denyssevysh T, Harasym T, Masin D, Tardi P, **Mayer LD** and Bally MB (2004) "Drug Ratio Dependence of Combination Chemotherapy: Use of Delivery Vehicles to Optimize Therapeutic Effects" American Association for Cancer Research 95th Annual Meeting, Orlando, Florida, March 27-31, 2004. Proceedings of the American Association of Cancer Research 51 #148
52. Johnstone S, Harvie P, Shew C, Kadhim S, Harasym T, Tardi P, Harasym, N and **Mayer, LD** (2005) "Synergistic antitumor activity observed for a fixed ratio liposome formulation of Cytarabine (Cyt.): Daunorubicin (Daun) against preclinical leukaemia models" April 2005. Proceedings of American Association of Cancer Research 52 #329
53. Johnstone S, Harvie P, Kadhim S, Harasym T, Tardi P, Harasym N and **Mayer LD** (2006) "Cytarabine (Cyt): Daunorubicin (Daun) combined inside liposomes at a fixed synergistic ratio leads to potent therapeutic activity against a range of preclinical leukaemia models" April 2006. Proceedings of the American Association of Cancer Research 53 #720

PATENTS

Granted

1. US Patent # 4,975,282 (1990), "Multilamellar Liposomes having Improved Trapping Efficiencies", Inventors: Cullis, P.R., Bally, M.B., Hope, M.J., Janoff, A.S. and **Mayer, L.D.**
2. US Patent # 5,077,056 (1991), "Encapsulation of Antitumour Agents in Liposome(s) After Generating Trans-membrane Potential", Inventors: Bally, M.B., Cullis, P.R., Hope, M.J., Madden, T.D., **Mayer, L.D.** and Loughrey, H.
3. European Patent # 0295248 (1993 & 1999), "Liposome Preparation and Antibiotic", Inventors: Bally, Marcel, B.; Bolcsak, L.E., Cullis, P.R., Janoff, A.S., **Mayer, L.D.**, Lenk, R.P., Jedrusiak, J.A.
4. European Patent # 0191824 (1993), "Encapsulation of Antineoplastic Agents in Liposomes", Inventors: Bally, M.B., Cullis, P.R., Hope, M.J., Madden, T.D. and **Mayer, L.D.**
5. European Patent # 0231261 (1994), "Multilamellar Liposomes having Improved Trapping Efficiencies", Inventors: Cullis, P.R., Bally, M.B., Hope, M.J., Janoff, A.S. and **Mayer, L.D.**
6. US Patent # 5,409,704 (1995), "Liposomes Comprising Aminoglycoside Phosphates and Methods of Production and Use", Inventors: Bally, M.B., Bolcsak, L.E., Cullis, P.R., Janoff, A.S., **Mayer, L.D.**
7. European Patent # 0290296 (1996), "Liposomal Formulations with a High Antineoplastic Agent/Lipid Ratio" Inventors: Bally M.B., Ginsberg R.S., Mitlenes G.N., Cullis P.R., **Mayer, L.D.**
8. European Patent # 0498471 (1996), "Liposomes Comprising a Guanidino Aminoglycoside", Inventors: Bally, M.B., Bolcsak, L.E., Cullis, P.R., Janoff, A.S., **Mayer, L.D.**, Lenk, P.R., Jedrusiak, A.J.
9. US Patent # 5,543,152 (1996), "Sphingosomes for Enhanced Drug Delivery", Inventors: Webb M.S., Bally M.B., **Mayer L.D.**
10. US Patent # 5,595,756 (1997) "Liposomal Compositions for Enhanced Retention of Bioactive Agents", Inventors: Bally, M.B., Boman, N.C., Cullis, P.R., **Mayer, L.D.**
11. US Patent # 5,616,341 (1997), "High Drug: Lipid Formulations of Liposomal-Antineoplastic Agents", Inventors: **Mayer L.D.**, Bally M.B., Cullis P.R., Ginsberg R.S., Mitlenes G.N.
12. US Patent # 5,736,155 (1998), "Encapsulation of Antitumour Agents in Liposomes", Inventors: Bally, M.B., Cullis, P.R., Hope, M.J., Madden, T.D., and **Mayer, L.D.**
13. US Patent # 5,741,516 & 5,814,335 (1998), "Sphingosomes for Enhanced Drug Delivery", Inventors: Webb M.S., Bally M.B., **Mayer L.D.**, Miller J.J., Tardi P.G.

14. US Patent # 5,744,158 (1998), "Methods of Treatment Using High Drug-Lipid Formulations of Liposomal-Antineoplastic Agents", Inventor: **Mayer L.D.**, Bally M.B., Cullis P.R., Ginsberg R.S., Mitlenes G.N.
15. US Patent # 5,795,589 (1998), "Liposomal Antineoplastic Agent Compositions", Inventors: **Mayer L.D.**, Bally M.B., Cullis P.R., Ginsberg R.S., Mitlenes G.N.
16. US Patent # 6,011,041 (2000) "Use of Anhydrovinblastine" Inventors: Schmidt, B., Kutney, J., **Mayer L.D.**
17. US Patent # 6,083,530 (2000) "High Drug: Lipid Formulations of Liposomal-Antineoplastic Agents", Inventors: **Mayer L.D.**, Bally M.B., Cullis P.R., Ginsberg R.S., Mitlenes G.N.
18. US Patent # 6,326,376 (2001) "Anhydrovinblastine for the Treatment of Cancer", Inventors: Schmidt B., Kutney, J., **Mayer L.D.**
19. European Patent # 0719546 (2003) "LUV Comprising Saturated Phospholipids and Method of Making the Same", Inventors: Bally M.B., Cullis P.R., Ginsberg R.S., **Mayer L.D.**, Mitlenes G.N.
20. European Patent # 0804159 (2003) "Sphingosomes for Enhanced Drug Delivery", Inventors: Webb M.S., Bally M.B., **Mayer L.D.**, Miller J.J., Tardi P.G.
21. European Patent # 0969839 (2003) "Anhydrovinblastine for the Treatment of Cancer", Inventors: Schmidt B., Kutney, J., **Mayer L.D.**
22. European Patent #1432402 (2006) "Compositions for Delivery of Drug Combinations", Inventors: Tardi, P., Harasym, T., Webb, M., Shew, C., **Mayer, L.D.**, Bally, M.B., Janoff, A.S.

Applications

1. EP Patent Application # 472639 (filed 1990), WO Patent Application #9014105, "Liposome Compositions Containing Drugs - Where Liposome(s) Have Trans-membrane Ion Gradient", Inventors: Madden, T.D., Hope, M.J., Tilcock, C.P., Cullis, P.R., Harrigan, P.R., Mui, B.S., Tai, L. and **Mayer, L.D.**
2. US Patent Application # 20030124181 (filed 2002) "Lipid Carrier Compositions with Enhanced Blood Stability", Inventors: Webb, M., Tardi, P., **Mayer, L.D.**, Ickenstein, L.
3. US Patent Application # 20040265368 (filed 2004) "Combination Compositions of Camptothecins and Fluoropyrimidines", Inventors: **Mayer, L.D.**, Bally, M.; Webb, M.; Tardi, P.; Johnstone, S.
4. US Patent Application # 20060228694 (filed 2004) "Methods to Individualize Combination Therapy", Inventors: Janoff, A., **Mayer, L.D.**, Bally, M.
5. US Patent Application # 20070031480 (filed 2004) "Enhanced Delivery of Sphingolipids", Inventors: **Mayer, L.D.**, Shabbits, J., Bally, M.
6. WO Patent Application # 04087105 (filed 2004) "Combination Formulations of Platinum Agents and Fluoropyrimidines", Inventors: **Mayer, L.D.**, Bally, M, Webb, M., Tardi, P., Shew, C.

7. WO Patent Application # 05102359 (filed 2005) "Combination Formulations of Anthracycline Agents and Cytidine Analogs", Inventors: **Mayer, L.D.**, Johnstone, S., Harasym, T.
8. US Patent Application # 20060165577 (filed 2005) "Compositions for Delivery of Drug Combinations", Inventors: Tardi, P., Harasym, T., Webb, M., Shew, C., **Mayer, L.D.**, Bally, M.B., Janoff, A.S.
9. US Patent Application # 20070286897 (filed 2005) "Liposomal Formulations of Anthracycline Agents and Cytidine Analogs", Inventors: **Mayer, L.D.**, Johnstone, S., Harasym, T.
10. WO Patent Application # 06014626 (filed 2005) "Particulate Constructs for Release of Active Agents", Inventors: **Mayer, L.D.**, Prud'homme, R., Allen, C., Saad, W.
11. WO Patent Application # 06055903 (filed 2005) "Method for Loading Multiple Agents into Delivery Vehicles", Inventors: **Mayer, L.D.**, Webb, M., Tardi, P., Johnstone, S., Harvie, P.
12. WO Patent Application # 06081354 (filed 2006) "Lipid Carrier Compositions with Reduced Polydispersity", Inventors: Tardi, P., **Mayer, L.D.**, Cabral-Lilly, D.
13. WO Patent Application # 07035783 (filed 2006) "Combination Formulations of Cytidine Analogs and Platinum Agents", Inventors: Johnstone, S., Harvie, P., Tardi, P., Harasym, T., **Mayer, L.D.**
14. WO Patent Application # 07050784 (filed 2006) "Fixed Ratio Drug Combination Treatments for Solid Tumors", Inventors: Janoff, A., **Mayer, L.D.**, Redman, J., Swenson, C.
15. WO Patent Application # 07064978 (filed 2006) "Localized Delivery of Drug Combinations", Inventor: **Mayer, L.D.**
16. WO Patent Application # 07076117 (filed 2006) "Liposomal Formulations Comprising Secondary and Tertiary Amines and Methods of Preparing Thereof", Inventors: Dicko, A., Tardi, P., **Mayer, L.D.**, Johnstone, S.